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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/695,275	10/28/2003	Bob G. Sanders	CLFR:178USD1	4689

7590 08/01/2006

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EXAMINER	
KHARE, DEVESH	
ART UNIT	**PAPER NUMBER**
1623	

DATE MAILED: 08/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/695,275	SANDERS ET AL.	
	Examiner	Art Unit	
	Devesh Khare	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8,14-16,18-24,34-38,40-48,58-62 and 64-67* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8,14-16,18-24,34-38,40-48, 58-62 and 64-67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

The amendments and remarks received on 06/23/2006 have been entered in view of the RCE request. Claims 1,14,18-24,40-48,64 and 65 have been amended. New claims 66 and 67 have been added. Claims 7, 9-13, 17, 25-33,39, 49-57 and 63 have been cancelled previously. The finality of the Office Action mailed on 03/06/2006 has been withdrawn.

The rejection under 35 U.S.C 112, first paragraph of the office action dated 03/06/2006 has been withdrawn in favor of the new grounds of rejection in response to the applicant's amendments dated 06/23/2006 presented in the following rejection under 35 U.S.C. 112, first paragraph.

During the course of reconsideration of the application, a prior art reference not previously disclosed by the applicants or the examiner came to light (see rejection below).

An action on the merits of claims 1-6,8,14-16,18-24,34-38,40-48, 58-62 and 64-67 is contained herein below.

Specification

The disclosure is objected to because of the following informalities:

The status of the related application cited at the first page of the specification should be updated to ensure a properly completed file record. This application lacks the necessary reference to the issued U.S. Patent No. 6,703,384 which was issued to the parent application serial no. 10/008,066 filed 11/05/2001.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6,8,18-24,34-38,40,41 and 66 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in **scope** with the claim with respect to with respect to inhibiting **any** tumor cell in an individual broadly in claims 1-6, and/or those numerous tumors listed in claim 8.

Note that **any** tumor cell growth would reasonably broadly encompass those known and unknown tumors as of the instant filing date, as well as those future known compounds yet to be discovered and diagnosed.

The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without ***undue experimentation***. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims;

(6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

1. The nature of the invention: The instant invention pertains to a method of inhibiting any tumor cell in an individual including those numerous tumors listed in claim 8 comprising administering to the individual a pharmacolologically effective dose of the instant compound of claim 1.

2. The state of the prior art: The skilled artisan would view tumors as a group of maladies (cancers) not treatable with one medicament or therapeutic regimen. Treatment efforts and efforts to cure all tumors (cancers) have produced only isolated identifiable positive results. See *In re Application of Hozumi et al.*, 226 USPQ 353. Moreover, it is well known that so far no single chemotherapeutic agent has been found to be useful in the treatment of **all** cancers, or even useful in the treatment of all types of breast cancers; and colon cancers; and prostate cancers; and leukemias. For example, breast cancers and leukemia do not share a common cause and differ in their methods of treatment, i.e., breast cancers are routinely with estrogens, antiestrogens, and/or androgens, unlike leukemia which is routinely treated with l-asparaginase, daunorubicin, and purine analogs.

3. The predictability of the art, and the breadth of the claims: Note that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Moreover, it is known that repeated therapeutic failures, after promising in-

vitro test results, suggest to the skilled artisan that claims based on in-vitro data, directed to treating cancer generally, are highly unpredictable, as taught in Trisha Gura's article in *Science*, November, 1997:

"[T]he institute started by pulling together mouse models of three tumors: a leukemia, which affects blood cells; a sarcoma, which arise in bone, muscle, or connective tissue; and carcinoma, the most common cells and includes such major killers as breast, colon, and lung cancers. Initially, many of the agents tested in these models appeared to do well. However, most worked against blood cancers such as leukemia and lymphoma, as opposed to the more common solid tumors. And when tested in human cancer patients, most of these compounds failed to live up to their early promise." (emphasis added, see for example, the middle column of the article).

Based on the known teachings of the cancer treatment such as in Trisha Gura's reference, one of skill in the art would recognize that it is highly unpredictable in regard to the treatment in the instant case, including treating numerous and various tumors: tumor cells comprising ovarian cancer, a cervical cancer, an endometrial cancer, a bladder cancer, a lung cancer, a breast cancer, a testicular cancer, a prostate cancer, a glioma. A fibrosarcoma, a retinoblastoma, a melanoma, a soft tissue sarcoma, an osteosarcoma, a leukemia, a colon cancer, a carcinoma of the kidney, a pancreatic cancer, a basel cell carcinoma, or a squamous cell carcinoma, by administering the very same compound.

4. The presence of absence of working examples: naturally occurring tocopherols and tocotrinols and the synthetic derivatives thereof were tested in vitro for their tumor growth inhibitory properties and for inducing apoptosis (see the Examples 4-20 and the Table 2-1, 2-2,3-1 and 3-2 at page 95 to page 98 of the specification).Thus,

the evidence in the examples is **not** commensurate in **scope** with the claimed invention and does not demonstrate criticality of a claimed range of the compounds of claim 1 and numerous and various tumors in the claimed method. See MPEP § 716.02(d).

Further, those unknown or future known tumors must require additional or future research to discover and diagnose. Therefore, the skilled artisan has to exercise **undue experimentation** to practice the instant invention.

Thus, the specification fails to provide sufficient support of the broad use of the compounds for inhibiting the growth of tumor cells in an individual including numerous and various tumors recited in the instant claims. As a result, necessitating one of skill to perform an exhaustive search for the embodiments of compounds and tumors encompassed by the instant claims suitable to practice the claimed invention.

Genentech, 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the *Wands* factor and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in *undue experimentation* to test compounds and tumors encompassed in the instant claims, with no assurance of success.

35 U.S.C. 103(a) rejection

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a

whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-6,8,14-16,18-24,34-38,40-48, 58-62 and 64-67 are rejected under 35 U.S.C. 103(a) as being obvious over Sanders et al. (U.S. Patent 6,770,672) ('672) and Sanders et al. (U.S. Patent 6,417,223) ('223).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Both the '672 and '223 patents teach a method for the treatment of a cell proliferative disease in an animal comprising administering to an animal a pharmacologically effective dose of a tocopherol compound and a method of inducing apoptosis of a cell, comprising the step of contacting said cell with a pharmacologically effective dose of a tocopherol compound ('672: col.3, lines 21-65 and '223: col.3, lines 16-54). Both patents disclose the use of α-,β- and δ- tocopherols ('672: col.2, lines 15-25). It is noted that the R^5 group of the compounds in the prior arts '672 and '223 patents is "phytyl" group (or a saturated phytyl side chain) ('672: col.2, lines 21-23 and see the general structure of the compound at col.2, line 60) whereas in the instant compounds the R^5 group is an unsaturated isoprenyl side chain. It would have been obvious to one skilled in this art to modify the R^5 group of the tocopherol compounds of said prior arts having same utility with a reasonable expectation of success. Also, the compound of instant claims 3 and 16 is obvious over 2,5,78-tetramethyl-2-R-(4,8,-dimethyl-1,3,7 EZ nonotrien)chroman-6-yloxy) acetic acid (26) of the prior arts due to same core structure ('672: col.5, lines 65-67). The prior arts '672 and '223 patents disclose that the derivatives of both tocopherols and tocotrienols compounds are effective as pro-apoptoic and DNA synthesis agents ('672: col.2, lines 15-17 and col.5, lines 26-33). The prior arts disclose that the derivatives of tocopherols and tocotrienols compounds can be used in the treatment of neoplastic diseases such as ovarian cancer, prostate cancer, glioma and endometrial cancer ('672: col.6, lines 47-59). The '672 and '223 patents disclose the dosage of said compounds between 0.1 mg/kg to 100 mg/kg and various administration

modes such as oral, topical, intraocular, parenteral and intravenous are also disclosed ('672: col.7, lines 27-35).

The prior arts is silent with regard to the specific tocotrienol compounds wherein R^5 group is an unsaturated isoprenyl side chain claimed in the instant method claims, however it would be within the scope of the artisan in this art to modify the R^5 group of tocopherol compounds to accomplish tocotrienol compounds through routine experimentation because the '672 and '223 patents disclose that both tocopherols wherein R^5 group is a "phytyl" group and tocotrienols compounds wherein R^5 group is an unsaturated isoprenyl side chain, are effective as pro-apoptoic and DNA synthesis agents.

It would have been obvious to person having ordinary skill in the art at the time the invention was made, to modify the R^5 group of tocopherol compounds of said prior arts to accomplish instant tocotrienol compounds through routine experimentation because the '672 and '223 patents teach that these compounds are known to be used for the same method that is being claimed. The motivation is provided by the '672 patent, the prior art suggests that the derivatives of both tocopherols and tocotrienols compounds are effective as pro-apoptoic and DNA synthesis agents ('672: col.2, lines 15-17 and col.5, lines 26-33). The applicant failed to show any unexpected results with the use of said tocotrienol compounds wherein R^5 group is an unsaturated isoprenyl side chain, in a method for inhibiting the growth of tumor cells in an individual and in a method of inducing apoptosis of a cell.

Any inquiry concerning this communication or earlier communications from the

Examiner should be directed to Devesh Khare whose telephone number is (571)272-0653. The examiner can normally be reached on Monday to Friday from 8:00 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anna Jiang, Supervisory Patent Examiner, Art Unit 1623 can be reached at (571)272-0627. The official fax phone numbers for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Devesh Khare, Ph.D.,J.D.
Art Unit 1623

July 24, 2006